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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/155,252	09/21/1998	RONALD MARK EVANS	SALK1470-2	8370

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EXAMINER	
BUNNER, BRIDGET E	

ART UNIT	PAPER NUMBER
1647	

DATE MAILED: 04/05/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/155,252	EVANS ET AL.	
	Examiner	Art Unit	
	Bridget E. Bunner	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 December 2003*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *16,18-20 and 27-45* is/are pending in the application.

4a) Of the above claim(s) *29-35* is/are withdrawn from consideration.

5)☒ Claim(s) *16,18-20,28,43 and 45* is/are allowed.

6)☒ Claim(s) *27,36,37,39-42 and 44* is/are rejected.

7)☒ Claim(s) *38* is/are objected to.

8)☒ Claim(s) *16, 18-20, 27-45* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☒ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of Application, Amendments and/or Claims

The amendment of 05 December 2003 has been entered in full. Claims 27-28, 36, and 44-45 are amended.

This application contains claims 29-35 drawn to a non-elected invention. Since applicant had received an action on the merits for the originally presented invention, this invention was constructively elected by original presentation for prosecution on the merits. Please see pg 2 of Office Action 26 February 2003. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claims 16, 18-20, 27-28, and 36-45 are under consideration in the instant application.

Withdrawn Objections and/or Rejections

1. The rejections to claims 28 and 45 under 35 U.S.C. § 103(a), as set forth at pg 6-11 of the previous Office Action (05 September 2003) are *withdrawn* in view of Applicant's persuasive arguments (05 December 2003). It is noted that the references cited by the Examiner do not teach the claim limitation of contacting cells with at least one additional compound that is a PPAR-γ antagonist.

Oath/Declaration

2. The objection to the declaration regarding the issue of not identifying the post office address of each inventor is maintained and held in abeyance until allowable subject matter is identified (see the Office Action of 15 August 2001, Paper No. 17).

Claim Objections

3. Claim 38 is objected to as being dependent upon a rejected base claim.

Claim Rejections - 35 USC § 102

4. Claim 27 is rejected under 35 U.S.C. 102(b) as being anticipated by Marcus et al. (Proc Natl Acad Sci USA 90: 5723-5727, 1993). The basis for this rejection is set forth at pg 3-4 of the previous Office Action (05 December 2003) and at pg 3-4 of the Action of 26 February 2003.

Applicant's arguments (05 December 2003), as they pertain to the rejections have been fully considered but are not deemed to be persuasive for the following reasons.

Applicant asserts that the invention of the instant application is distinguishable over Marcus by requiring contacting the test cells with at least two compounds. Applicant argues that the language of the claim makes it clear that two exogenous compounds were contemplated because the second must be a known PPAR-γ agonist. Applicant contends that Marcus does not teach or suggest contacting PPAR-γ-containing cells with at least two compounds as a method of evaluating a test compound for its ability to regulate transcription-activating effects of PPAR-γ.

Applicant's arguments have been fully considered but are not found to be persuasive. Specifically, Marcus teaches cotransfecting COS-1 cells with a PPAR-γ receptor expression vector and a reporter vector and contacting the cells with ciprofibrate, or Wy-14,643, wherein the substances caused an increase or decrease in the level of luciferase reporter protein (pg 5724-

5725; pg 5726; Figures 1 and 6). Marcus also teaches that COS cells may contain endogenous factors that activate mouse and rat PPAR, but not *Xenopus* PPAR (pg 5725, lines 1-3 and first and second full paragraphs). The Examiner acknowledges that Marcus does not teach contacting the cells with two exogenous compounds. However, claim 27 does not recite that compounds the compounds utilized are exogenous or endogenous. Simply reciting "contacting cells containing said receptor and reporter vector with (i) a test compound and (ii) at least one additional compound that is a PPAR-γ agonist" still encompasses endogenous compounds which are taught by Marcus.

Claim Rejections - 35 USC § 103

5. Claims 36-37 and 39-42 are rejected under 35 U.S.C. 103(a) as being unpatentable over Webster et al. (Cell 54:199-207, 1988) in view of Greene et al. (U.S. Patent 6,200,802). The basis for this rejection is set forth at pg 4-6 of the previous Office Action (05 September 2003) and at pg 4-6 of the Action of 26 February 2003.

Applicant's arguments (05 December 2003), as they pertain to the rejections have been fully considered but are not deemed to be persuasive for the following reasons.

Applicant argues that the invention of the instant application is directed to a method of testing a compound for its ability to regulate PPAR-γ. Applicant states that Webster merely uses known receptor activators in a mechanistic study to localize the activation domains of the human estrogen or glucocorticoid receptors. Applicant asserts that Webster does not teach or suggest the use of GAL4-PPAR-γ chimeras to test compounds for PPAR-γ regulation. Applicant submits that Greene is unable to cure the deficiencies of Webster because it does not teach or suggest the use of GAL4-PPAR-γ chimeras to test compounds for PPAR-γ regulation. Applicant states that

Greene relates to the identification of PPAR-γ receptors. Applicant also points out that Webster uses known activators to study receptor activation because the goal of Webster is to localize functional activation domains. Applicant argues that the presence of an unknown or test compound would be completely antithetical to the desired goal because a change in activation could no longer be attributed solely to the receptor domains being studied. Applicant contends that Greene does not mention the use of any bioassay. Applicant asserts that the present invention focuses on identifying novel PPAR-γ modulators, i.e., testing compounds for their ability to modulate PPAR-γ. Applicant submits that in the instant application, chimeric GAL4-PPAR-γ receptors have been used in the identification of novel compounds capable of regulating PPAR-γ from a pool of uncharacterized test compounds in an assay format amenable to high-throughput screening.

Applicant's arguments have been fully considered but are not found to be persuasive. Specifically, Webster teaches a standard method of testing a compound for its ability to regulate transcription-activating effects of estrogen and glucocorticoid receptors by assaying for the changes in the level of CAT reporter protein present as a result of contacting cells containing GAL4 chimeric estrogen/glucocorticoid receptors and a reporter vector with the compound (pg 200, col 2; Figure 2-3; pg 202, last ¶ of col 2 through 203). Webster also teaches a reporter vector that comprises rabbit β-globin promoter, two synthetic 17-mer GAL4 DNA binding sites, and a DNA segment that encodes the CAT reporter protein (pg 200, col 2; Figure 3(A)). Webster teaches cotransfecting HeLa cells with the receptor expression vector and reporter vector and contacting the cells with hormones and anti-hormones wherein the substances caused an increase or decrease in the level of CAT reporter protein (pg 202-203; Figure 3(B)-3(C)).

Greene teaches the nucleic acid sequence and amino acid sequence of the human PPAR-γ receptor. Greene also discloses several domains of PPAR-γ, such as the D domain or ligand binding domain (col 14, Figure 1). It would have been obvious to the person of ordinary skill in the art at the time the invention was made to modify the GAL4 chimeric receptor/reporter vector method for testing the transcription activation of a compound as taught by Webster by substituting the estrogen/glucocorticoid receptor with the PPAR-γ receptor as taught by Greene. Furthermore, since Webster teaches a standard assay for testing compounds for their ability to regulate transcription-activating effects, the same compounds utilized by Webster (i.e., hormones, anti-hormones) can be used with the PPAR-γ receptor as taught by Greene. Additionally, the feature upon which Applicant relies (contacting cells with a novel compound), is not recited in the rejected claims. Applicant states that the claims have been amended to clarify that the method comprises "contacting cells containing a GAL4 chimeric PPAR-γ receptor and a reporter vector with a test compound". However, a test compound does not necessarily have to be a novel compound.

6. Claim 44 is rejected under 35 U.S.C. 103(a) as being unpatentable over Webster et al. (Cell 54:199-207, 1988) in view of Greene et al. (U.S. Patent 6,200,802) and Ikonen et al. (Endocrinology 135: 1359-1366, 1994). The basis for this rejection is set forth at pg 8-11 of the previous Office Action (05 September 2003).

Applicant's arguments (05 December 2003), as they pertain to the rejections have been fully considered but are not deemed to be persuasive for the following reasons.

Applicant asserts that, as discussed above, Webster does not teach or suggest the use of GAL4-PPAR-γ chimeras to evaluate test compounds for PPAR-γ regulation. Applicant argues that Greene is unable to cure the deficiencies of Webster because it also does not teach or suggest the use of GAL4-PPAR-γ chimeras to test compounds for PPAR-γ regulation. Applicant contends that Ikonen is unable to cure the deficiencies of Webster because it does not teach or suggest the use of GAL4-PPAR-γ chimeras to test compounds for PPAR-γ regulation.

Applicant's arguments have been fully considered but are not found to be persuasive. As discussed above, Webster teaches a standard method of testing a compound for its ability to regulate transcription-activating effects of estrogen and glucocorticoid receptors by assaying for the changes in the level of CAT reporter protein present as a result of contacting cells containing GAL4 chimeric estrogen/glucocorticoid receptors and a reporter vector with the compound (pg 200, col 2; Figure 2-3; pg 202, last ¶ of col 2 through 203). Webster also teaches a reporter vector that comprises rabbit β-globin promoter, two synthetic 17-mer GAL4 DNA binding sites, and a DNA segment that encodes the CAT reporter protein (pg 200, col 2; Figure 3(A)). Webster teaches cotransfecting HeLa cells with the receptor expression vector and reporter vector and contacting the cells with hormones and anti-hormones wherein the substances caused an increase or decrease in the level of CAT reporter protein (pg 202-203; Figure 3(B)-3(C)). Greene teaches the nucleic acid sequence and amino acid sequence of the human PPAR-γ receptor. Greene also discloses several domains of PPAR-γ, such as the D domain or ligand binding domain (col 14, Figure 1). It would have been obvious to the person of ordinary skill in the art at the time the invention was made to modify the GAL4 chimeric receptor/reporter vector method for testing the transcription activation of a compound as taught by Webster by utilizing

the agonist/antagonist testing methods of Ikonen and by substituting Webster's estrogen/glucocorticoid receptor with the PPAR-γ receptor as taught by Greene. Furthermore, since Webster teaches a standard assay for testing compounds for their ability to regulate transcription-activating effects, the same compounds utilized by Webster (i.e., hormones, anti-hormones) can be used with the PPAR-γ receptor as taught by Greene. Additionally, the feature upon which Applicant relies (contacting cells with a novel test compound), is not recited in the rejected claims. A test compound does not necessarily have to be a novel compound.

In response to applicant's argument that there is no suggestion to combine the references, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988)and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). In this case, the person of ordinary skill in the art would have been motivated to modify the method of Webster because PPAR-γ is widely expressed in the human hematopoietic system (Greene et al., col 36-39) and the nuclear receptor subfamily to which the PPAR-γ receptor belongs has been shown to regulate the transcription of key enzymes in fatty acid metabolism and may play a role in cancer cell proliferation and differentiation (Greene et al., col 2). The person of ordinary skill in the art reasonably would have expected success because similar methods were already being performed to discover the transcription activating effects of various compounds on receptors at the time the invention was made. Therefore, the claimed invention as a whole was clearly *prima facie* obvious over the prior art.

Conclusion

Claims 16, 18-20, 28, 43, and 45 are allowable.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bridget E. Bunner whose telephone number is (571) 272-0881. The examiner can normally be reached on 8:30-4:30 M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Kunz can be reached on (571) 272-0887. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Elizabeth C. Kemmerer

BEB
Art Unit 1647
31 March 2004

ELIZABETH KEMMERER
PRIMARY EXAMINER